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DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

T-155-1 - Nicolle, C. - experimental reproduction of exanthematic typhus in monkeys. A note by M. Ch. Nicolle, presented by M. Roux.

We shall limit this first note to a condensed presentation of our experiments. The latter bring their own lesson. Exanthematic typhus, an ailment hitherto considered to be peculiar to man, could not, until now, be reproduced in animals. Its experimental study, which seemed to be impossible, has become practical thanks to inoculability to the monkey.

The material for the experiments was borrowed by us from a native afflicted with typhus and treated in the Rabta (Tunis) lazaret. Here is the observation of that patient according to information provided to us by Dr. Broc, whom we thank for his aid to our research.

Human observation. - M.B.K.D., 35 year old, entered Sadiki Hospital on May 14 for reason of vesical calculus, presented on May 17 a sudden rise in temperature; because of the typhus epidemic which was raging, he was at once sent to Rabta. As he entered that institution he was found to have a "roasted" tongue and to be constipated. On May 19 he was found to have face congestion, some stupor, and barely noticeable pink spots had erupted on his flanks; his pulse was 103; no albumine. Clear improvement began on the next day; the patient sat up in his bed. He left on the 27-th, at his own request.

Summing up: classical benign typhus lasting five days, whose temperature curve is given below.

On May 19, third day of infection, a few hours after the appearance of the eruption, we took from the vein of this patient 1 cm³ of blood, which we inoculated at once to a chimpanzee. That animal, after an incubation of 24 days (interrupted only by a slight rise in temperature lasting 2 days), has presented one of the clearest cases of typhus, as the following observation and the temperature curve which accompanies it show:

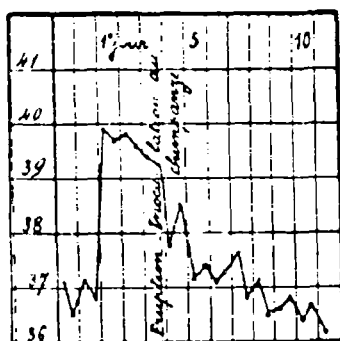


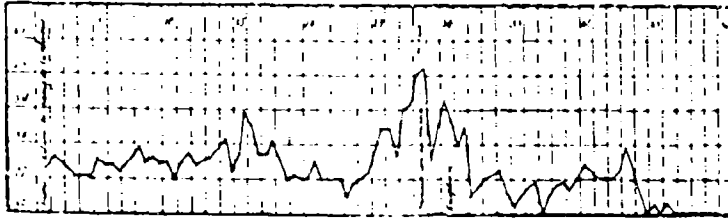
Figure 1.

(1st day. Eruption - Inoculation of chimpanzee)

M.B.K.D. temperature curve. Exanthematic typhus. Curve #1.

Observation of the chimpanzee: - It is a case of a young animal, which is a priori an unfavorable condition in view of the fact that, among humans, typhus is especially benign in the child and often passes unnoticed in it. Good health

Fig. 2



Curve II. (Chimpanzee).

(Inoculation with blood from a typhus patient

Inoculation of macacus sinicus

Eruption.

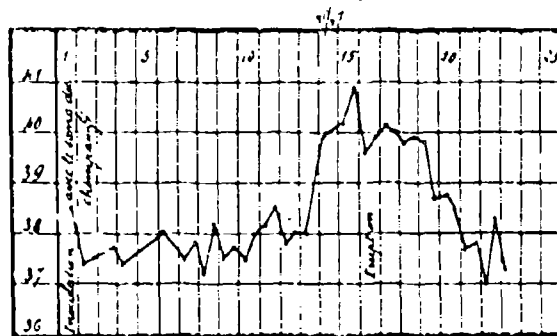
until June 12. On that day (the 25th since the inoculation), the temperature rose. It went above 40° on the 15th; on that date the general state of health remained good; the animal generally remained in a lying position, but got up to eat and drink. The eruption appeared on the 17th, in the form of black spots on the face, where they are difficult to see because of the pigmentation of the skin; they are, on the contrary, quite visible at the level of the ears. From the 18th on there was an aggravation of the general state of health, coinciding with a decrease in temperature; prostration; the chimpanzee does not get up, does not eat, or hardly eats; diarrhea. On the 27th day, dark red, poorly circumscribed large spots appear on the trunk. During the next days this eruption disappears, desquamation of hands, general thinning of the body occurring progressively, hypothermia. Briefly, the incubation lasted 24 days, a benign typhus (in its period of fever) lasting 7 days; eruption. Consecutive cachexia.

On June 15, the fourth day of the infection of the chimpanzee, while the temperature reaches $40^{\circ}.2$, and 2 days before the eruption, we took from the vein of that animal 1 cm³ of blood, ^{with} which we inoculated hypodermically a bonneted macaque (macaca) (Macacus sinicus). The latter, after an inoculation lasting 13 days, contracted a typical typhus, as it is proven by the following observation and curve:

Observation of the bonneted macaca. - Perfect general state of health until June 27, at which date the temperature rose, and same state lasting through the next two days. On June 30 (3rd day of infection), quick appearance of an eruption on the face, mainly at the level of the ears, of the nose root and of the palpebral areas, both frontal and malar. This eruption consists in bright red spots, confluent on the nose and isolated elsewhere; they disappear when pressed, only

to reappear as soon as pressure ceases. The animal is nervous, has feverish tremblings and remains in lying position; humid tongue; pulse 110. Same state the next day. The eruption abates during the following days, but does not completely disappear at the time the fever disappears, which occurs on the eighth day of the malady. Then the state of health is very good, the animal eats, but remains lying and is extremely emaciated. Presence of numerous epithelious cylinders in the urine.

Fig 3.



Curve III. (bonneted macaca.)

(Inscriptions in italics in the graph: Inoculation with chimpanzee's blood -- Eruption)

To sum up: classical typhus lasting 8 days, with some extremely characteristic eruptions.

Two attempts to inoculate the bonneted macaca directly with the patient's blood yielded negative results.

The experiments which we have reported prove:

- 1° The possibility of transmitting typhus from man to chimpanzee and, after passage through the latter, to a bonneted macaca of the common species.
- 2° The presence of virus in man's blood on the day of the eruption and in the chimpanzee's blood two days before the appearance of the eruption.

We present our thanks to the Institut Pasteur of Paris which, by putting a chimpanzee at our disposal, has made it possible to carry out our experiments.